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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/718,265	11/21/2003	David Hildebrand	50229-412	8133
7590 03/24/2006 MCDERMOTT, WILL & EMERY 600 13th Street, N.W. Washington, DC 20005-3096			EXAMINER CHOWDHURY, IQBAL HOSSAIN	
			ART UNIT 1652	PAPER NUMBER

DATE MAILED: 03/24/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/718,265	Applicant(s) HILDEBRAND ET AL.	
	Examiner Iqbal Chowdhury, Ph.D.	Art Unit 1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 09 January 2006.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-13 is/are pending in the application.
- 4a) Of the above claim(s) 4 and 8-13 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1 and 5-7 is/are rejected.
- 7) ☒ Claim(s) 2 and 3 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Application Status

In response to a previous Office action, a non-final requirement (mailed on September 8, 2005), Applicants filed a response and amendment received on January 9, 2006, amending claims 1-3 and 6, and withdrawing claims 4 and 8-13 is acknowledged. Claims 1-3 and 5-7 are pending in the instant Office action. Thus, claims 1-3 and 5-7 will be examined herein.

This application contains claims drawn to an invention nonelected with traverse in communication filed on 1/9/2006. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Withdrawn Claim Rejections - 35 U.S.C. § 112(2)

Previous rejection of claim 2 under 35 USC § 112, second paragraph, as being indefinite is withdrawn by virtue of Applicant's amendment to claim.

Previous rejection of claims 1-3 and 5-7 under 35 USC § 112, second paragraph, as being indefinite is withdrawn by virtue of Applicant's amendment to the claims.

Maintained - Claim Rejections - 35 U.S.C. § 112

Previous rejection of Claims 1 and 5-7 under 35 U.S.C. 112, first paragraph, enablement requirement, is maintained. This rejection has been described in length in previous Office Action. Applicant's arguments have been fully considered but are not deemed persuasive for the following reasons.

As mentioned in the previous Office Actions, claims 1 and 5-7 are so broad as to

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encompass any polynucleotide encoding a hydroperoxide lyase (HL) having at least 90% identity to an enzyme of SEQ ID NO: 1. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of hydroperoxide lyase (HL) broadly encompassed by the claims. The scope of the claimed invention is very broad in the context of at least 90% identity to SEQ ID NO: 1. How many polypeptides having hydroperoxide lyase activity can be encompassed by these claims?

Applicants argue that regions of protein structure which may be modified without affecting hydroperoxide lyase (HL) activity is known before filing of the present application and reciting two publications.

While methods to produce variants of a known sequence such as site-specific mutagenesis, random mutagenesis, etc. are well known to the skilled artisan, producing variants useful as hydroperoxide lyase (HL) requires that one of ordinary skill in the art know or be provided with guidance for the selection of which of the infinite number of variants have the activity. Without such guidance one of ordinary skill would be reduced to the necessity of producing and testing all of the virtually infinite possibilities. For the rejected claims, this would clearly constitute **undue** experimentation. Guo et al. (Protein tolerance to random amino acid change, Proc Natl Acad Sci U S A, 2004 Jun 22; 101(25): 9205-10, Epub 2004 Jun 14) teach that the percentage of random single substitution mutations which inactivate a protein for the protein 3-methyladenine DNA glycosylase is 34% and that this number appears to be consistent with other studies in other proteins as well. Guo et al. further show in Table 1 that the percentage of active mutants for multiple mutants appears to be exponentially related to this by the simple formula $(.66)^x \times 100\%$ where x is the number of mutations introduced. Applying this estimate to

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the instant protein 90% identity allows up to 48 mutations within the 481 amino acids of SEQ ID NO: 1 and thus only $(.66)^{48} \times 100\%$ or $2.2 \times 10^{-7}\%$ (i.e. $\cong 1$ in 500 million) of random mutants having 90% identity would be active. Similarly at 95% identity $4.7 \times 10^{-3}\%$ (1 in 21000). Current techniques (i.e., high throughput mutagenesis and screening techniques) in the art would allow for finding a few active mutants within several hundred thousand or up to about a million inactive mutants as is the case for the claims limited to 95% identity (despite even this being an enormous quantity of experimentation that would take a very long time to accomplish) but finding a few mutants within many millions or more as in the claims to 90% or less identity would not be possible. While enablement is not precluded by the necessity for routine screening, if a large amount of screening is required, the specification must provide a reasonable amount of guidance with respect to the direction in which the experimentation should proceed. Such guidance has **not** been provided in the instant specification.

Sufficient guidance has **not** been provided in the instant specification or in the prior art as at best art teaches to avoid changes of 10% of the structure of SEQ ID NO: 1 but does little to suggest what changes would be successful particularly for those enzymes having the substantial number of alterations necessary to produce a protein having 90% identity to SEQ ID NO: 1.

Conclusion

Claims 1 and 5-7 are rejected.

Claims 2 and 3 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

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Applicants must respond to the objections/rejections in each of the sections in this Office action to be fully responsive in prosecution. Accordingly, **THIS ACTION IS MADE FINAL**. See M.P.E.P., 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 C.F.R., 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 C.F.R., 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.


Any inquiry concerning this communication or earlier communications from the examiner should be directed to Iqbal Chowdhury, Ph.D. whose telephone number is 571-272-8137. The examiner can normally be reached on 9:00-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on 703-272-0928. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Respectfully,

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